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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,588	11/30/2001	Glenn J. Dorin	012441.00013	3451

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,588	DORIN ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-262* is/are pending in the application.

4a) Of the above claim(s) *129-262* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/30/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction Election

Applicant's election of Group I, claims 71-128 in the reply filed on May 18, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 129-262 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Therefore, claims 71-128 are currently pending and are under examination.

Objection to the Specification

The disclosure is objected to because of the following informalities:

1. The "$NaPO_4$" should be corrected to "Na_3PO_4" in Table 1 and in the specification.
2. The use of the trademarks "TWEEN" and "POLYSORBATE" have been noted in this application. They should be capitalized wherever they appear and placed within quotation marks and be accompanied by the generic terminology. See MPEP 608.01 (v). Appropriate correction is required.
3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Claim 71 and dependent claims 72-77 are directed to a solution comprising 200 mM to 300 mM arginine and a polypeptide selected from the group consisting of (i) human TFPI, (ii) ala-human TFPI, (iii) muteins of (i) and (ii) having from 1-5 amino acid substitutions. There is no mention of the ala-human limitation of TFPI in the specification. A correction is required.

Objection to the claims

1. Claims 79, 80 and 86 are objected to as to recite "concentration of from " A correction to read as "concentration from" would obviate the objection.
2. Claims 94-98 are objected to as to recite "concentration of." A correction to read as "concentration from" would obviate the objection.

Information Disclosure Statement

The information disclosure statement filed on November 30, 2001 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP 609 because the copies of the references listed in PTO Form 1449 were not submitted with the parent application 09/443099. Therefore the information referred to therein has not been considered as to the merits except in the US patents.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 71-128 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 71, 74, 77, 78, 108, 111 and 128 are indefinite regarding the terminology "TFPI", that should be spelled out fully at its first instance followed by the acronym/abbreviation within parentheses. Claims 72, 73, 75, 76, 79-107, 109, 110, 112-128 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend upon.

Claim 115 is indefinite as to read "concentration of at least about." It is not clear if the concentration of sodium chloride is 150mM or less than 150mM. Claims 116 and 117 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend upon.

Claim 118 is indefinite as to read "concentration of at least about." It is not clear if the concentration of sodium chloride is 500mM or less than 500mM. Claims 119 and 120 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend upon.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 71, 73, 78-80, 110 and 114 are rejected under 35 USC 102(b) as being anticipated by WO 93/25230 (December 23, 1993). WO'230 teaches LACI at a concentration of 3.5 mg/ml in combination with 150 mM NaCl and 20 mM sodium sulfate. WO'230 also teaches the use of isotonic NaCl as a carrier (see page 20, lines 25-26 and page 29, line 32). LACI is a synonym for TFPI. Inherently because LACI and NaCl are present in the same concentrations claimed by the applicants, the NaCl of WO'230 acts as a solubilizing agent/ stabilizer for LACI to the same extent claimed by the applicants.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections, set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 73, 85 and 118 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/25230. Application of WO'230 is the same as in the above rejection of claims 71, 73, 78-80, 110 and 114. WO'230 does not teach an LACI concentration of more than 3.5 mg/ml, does not teach NaCl concentrations of 0.5 M or greater, and does not teach pH's below 7.0 or 5.5. It would have been obvious to one of ordinary skill in the art at the time applicants' invention was made to form the LACI compositions of WO'230 having the concentrations and pH's outlined above because WO'230 is not limited to any particular concentrations or pH's (see page 29 line 1 to page 30 line 16) and discloses the need to optimize the concentrations depending upon the patient and mode of administration and because the concentration and pH are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical art.

Claims 71, 73, 78, 81-83, 86, 87, 89 and 95-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/25230 as applied against claims 71, 73, 78-80, 110 and 114 above, and further in view of Woog et al. WO'230 does not teach compositions including sucrose or glycine as stabilizers and solubilizers and including sodium phosphate as a buffer. Woog et al. teach that sucrose, polyethylene glycol and glycine are conventional stabilizers and solubilizers and that sodium phosphate and sodium citrate are conventional buffers for pharmaceutical compositions containing proteins (see column 7 lines 19-34, column 8 lines 43-51 and column 9 lines 1-14). Woog et al also teach arginine as the stabilizing or solubilizing agent (see column 9, lines 3-5). It would have been obvious to one of ordinary skill in the art at the time the applicants' invention was made to use in the LACI compositions of WO'230 the stabilizers,

solubilizers, and buffers of Woog et al. because WO'230 discloses that the LACI can be formulated according to the known art (see page 29 lines 24-37), because Woog et al. disclose stabilizers, solubilizers and buffers which are generally applicable to pharmaceutical compositions containing proteins, and because it would be desirable to stabilize, solubilize and buffer LACI so that it will maintain it's pharmaceutical activity. It would further have been obvious to one of ordinary skill in the art at the time the applicants' invention was made to determine all operable and optimal concentrations of the components in the compositions outlined above because the concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical composition art.

Claims 71 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/25230 as applied to claims 71, 73, 78-8-0, 110 and 114 above, and further in view of Patel. WO'230 does not teach histidine as a solubilizing agent. Patel teaches that histidine acts as a stabilizer for aqueous solutions of proteins including interferon, GM-CSF or interleukin. It would have been obvious to one of ordinary skill in the art at the time the applicants' invention was made to use in the LACI compositions of WO'230 the histidine of Patel as a stabilizer/ solubilizer, because Patel's histidine is generically applicable to all proteins (see column 1 lines 4-9), because a stabilizer which is operable for interferons, GM-CSF and interleukins would have been expected to be operable for all proteins because there is no structure in common among all interferons, GM-CSF and interleukins, because Patel's proposed stabilization mechanism (see column 3, lines 41-45) would be applicable to all proteins, and because it would be desirable to stabilize LACI so that it will maintain it's pharmaceutical activity.

Claims 72-77 and 79-110 are rejected as being dependent upon a rejected base claim.

Claim Rejections - Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 71, 73, 78, 79, 109 and 110 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 9, 33-35, 37 and 41 of U.S. Patent No. 6,323,326. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 71, 73, 78, 109 and 110 are directed to the broadest scope of the solution comprising a polypeptide selected from the group consisting of (i) human TFPI, (ii) ala-human TFPI and (iii) muteins of (i) or (ii). Claims 71, 73, 78, 109 and 110 encompass the TFPI amino acid sequences set forth in claims 1-3, 5 and 9; and encompass the ala-TFPI amino acid sequence set forth in claims 33-35, 37 and 41 of patent '326.

Claim 71 discloses a solution comprising from 200mM to 300 mM arginine, a polypeptide selected from the group consisting of (i) human TFPI, (ii) ala-human TFPI and (iii) muteins of (i) or (ii). This is an obvious variation of claims 1, and 33 in the patent '326, which discloses an aqueous formulation comprising TFPI and a charged polymer (claim 1 of '326) and wherein TFPI is Ala-TFPI (claim 33).

Claim 73 discloses a solution of claim 71 comprising from 0.2-10 mg/ml of said TFPI. This is an obvious variation of claims 1, 2 and 34 in the patent '326, which discloses an aqueous formulation comprising TFPI wherein the concentration of TFPI is greater than 1 mg/ml (claim 1 of '326), greater than 5 mg/ml (claim 2 of '326) wherein TFPI of claim 2 is Ala-TFPI (claim 34).

Claim 78 discloses a solution comprising more than 0.2 mg/ml of TFPI selected from the group consisting of (i) human TFPI, (ii) ala-human TFPI and (iii) muteins of (i) or (ii) and further comprising a solubilizer selected from the group consisting of sucrose....polyphosphate....and sodium dodecyle sulfate. This is an obvious variation of claim 9 and 41 in the patent '326, which discloses an aqueous formulation comprising TFPI and a charged polymer, wherein charged polymer is polyphosphate (claim 9 of '326) and wherein TFPI is Ala-TFPI (claim 41).

Claim 79 discloses a solution of claim 78 wherein the polypeptide is present in a concentration from 1-20 mg/ml. This is an obvious variation of claim 3 and 35 in the patent '326, which discloses an aqueous formulation of claim 1 ('326), wherein the concentration of TFPI is greater than 10 mg/ml (claim 3 of '326) and wherein TFPI is Ala-TFPI (claim 35).

Claim 109 discloses a solution of claim 108, which is pharmaceutically acceptable. This is an obvious variation of claim 5 and 37 in the patent '326, which discloses an aqueous formulation of claim 1 ('326), which is pharmaceutically acceptable (claim 5 of '326), and wherein TFPI is Ala-TFPI (claim 37).

Claim 110 discloses a solution of claims 78-107, which is pharmaceutically acceptable. This is an obvious variation of claim 5 and 37 in the patent '326, which discloses an aqueous formulation of claim 1 ('326), which is pharmaceutically acceptable (claim 5 of '326), and wherein TFPI is Ala-TFPI (claim 37).

Thus, claims 71, 73, 78, 79, 109 and 110 in present application and claims 1-3, 5, 9, 33-35, 37 and 41 in the patent '326 are obvious variations of a solution comprising, a polypeptide selected from the group consisting of (i) human TFPI, (ii) ala-human TFPI and (iii) muteins of (i) or (ii), wherein the solution comprises a solubilizer/stabilizer.

Conclusion

No claims are allowable.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Jon Weber, can be reached at (571) 272-0925. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette,1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

Rita Mitra, Ph.D.
August 4, 2004

Supervisory Jon P. Weber, Ph.D.
Primary Examiner